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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,320	06/12/2001	Ajay Hasmukhlal Upadhyay	RD 01022	5176

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EXAMINER	
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ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/879,320	UPADHYAY, AJAY HASMUKHLAL	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 6-8, 31 and 33-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,6-8,31 and 33-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of response and amendment dated 11-17-08 is acknowledged.

Claims 38-42 are new. Claims 1-4, 6-8, 31 and 33-42 are pending.

The following rejection is applied to the instant claims:

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-8, 31 and 33-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,372,252 to Blume et al (Blume) in view of US 5,032,406 to Dansereau et al (Dansereau), US 3627583 to Troy et al and Ansel et al (Pharmaceutical dosage forms). **New claims 38-42 are also rejected in this section.**

Blume teaches immediate and sustained release formulations comprising guaifenesin. Blume teaches loading guaifenesin and methocel into a high shear mixer, mixed at high speed, adding water and further mixing at additional time to complete granulation. The composition is next dried in fluid dryer and then passed through a mill fitted a suitable size screen (col. 7, lines 63 through col. 8, lines 23). Thus, the resulting material of Blume reads on agglomerated mixture because the processing of the material involves the same steps as described in the instant application.

Blume fails to teach granulation of guaifenesin with polyvinylpyrrolidone.

Dansereau teaches a tablet composition that provides dual action, for immediate and sustained release, comprising an outer tablet and an inner tablet respectively. The active ingredient of both inner and outer tablets comprises guaifenesin. The inner tablet

particularly comprises guaifenesin and polyvinylpyrrolidone (PVP) (example I).

Dansereau teaches that the inner tablet is made as follows (col. 6):

> The inner tablet is made by oscillating guaifenesin and half of the polyvinylpyrrolidone through a 30 mesh screen. The blend is then transferred to a pharmaceutical grade blender and mixed until it is of uniform consistency. It is then granulated with polyvinylpyrrolidone that had been previously dissolved in a sufficient amount of purified water to make a solution of from about 8% to about 12% of polyvinylpyrrolidone. This mixture is discharged and dried in a forced air oven at 40° C. until the water content is less than 1%. The dried granulation is then oscillated through a 12 mesh screen and returned to the blender. The remaining polyvinylpyrrolidone, microcrystalline cellulose and talc are added to this dried granulation and mixed until it is of uniform consistency. Finally, zinc stearate is added and the mixture is mixed until it is of uniform consistency. This mixture is then compressed into inner tablets using a standard tableting press.

Thus, the resulting inner tablet composition of Dansereau read on the claimed agglomerate mixture because the process involves the same steps as described in the instant specification (page 3, lines 15-20). Dansereau fails to teach the claimed particle sizes.

Troy teaches tablets formed by direct compression from a mixture of an active material such as therapeutic material and as a direct compression vehicle dry, free-flowing, granular sugar and a binder (abstract). Troy teaches that in order to obtain free-flowing particles of 12 mesh to 325 mesh (col. 1, L 50-65). Troy states that tablets result in good physical properties and readily dissolve in aqueous media (col. 1 and col. 4, L

1-10). Troy suggests mixing sugar and the binder to effect agglomeration of about 325 mesh (44 microns according to the declaration submitted by applicants on 10-26-07) but not greater than 12 mesh (col. 3, L 7-15 and lines 46-61). Among the active agents, Troy suggests antitussives but does not explicitly state employing guaifenesin.

Ansel et al teaches manufacturing of compressed tablet by different procedures such as wet granulation, dry granulation, and direct compression and states that the important requirement in tablet manufacture is a free-flowing drug from the hopper to the dies to enable high speed compression of powdered drug (page 209). In each of the types of compression tablet manufacture, Ansel teaches sizing the granules for free-flowing of drug and reduced capping (page 211, page 213 slugging and page 216). Ansel states that one reason for capping of tablets is the granulation which has too great a proportion of fines or fine powder (page 216, col. 2 and page 217).

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention from the teachings of Troy and Ansel that particle sizes of 12 mesh to 325 mesh are important for free flowing and the ability for compression, too fine a powder causes capping and while sizing of the granules particles is important for free flowing of drug. Ansel, Troy as well as Dansereau recognize PVP as a suitable binder for compressible tablets, particularly guaifenesin (Dansereau). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to employ PVP for the processing and preparation of compressible guaifenesin tablets of Blume because Ansel, Troy as well as Dansereau recognize PVP as a suitable binder and Dansereau recognizes methylcellulose (Blume) and PVP as

equivalent binders as well as disintegrants in preparing a sustained release compressible tablet preparation comprising guaifenesin.

With respect to the claimed particle sizes (including new claim 38, 42 and amended claim 37), Blume teaches that no more than 30% granulation material passes through 100 mesh (150 microns) and not more than 10% retained on 10-mesh screen (greater than 850 microns). Thus, majority of the particles of Blume are in the range of 150 microns – 2 mm and a smaller percentage of particles are below 150 microns. A maximum of 30% of the particles that pass through the 100-mesh screen, according to Blume, could be any size below 150 microns (as low as 45 microns claimed in the instant invention). While Blume does not teach the exact percentages of particle sizes claimed in the instant application, there is an overlap in the particle sizes between instant application and that of Blume (150 nm to 425 nm). Instant claims (except for claims 7 and 35) do not state the distribution of particle sizes between 45 microns and 425 microns. On the other hand, Ansel suggests free flowing particles of appropriate size (not too fine a powder) that do not exhibit capping are important and Troy suggests a particle size of 12 mesh (1.41 mm) to 325 mesh (44 microns) as suitable for free flowing, stable and compressible tablets. Accordingly, a skilled artisan would have readily optimized the particle sizes of the granulated PVP and guaifenesin between 12 mesh and 325 mesh sizes such that the particles have an optimum flow rate, strength and stability and yet do not show capping.

For the claimed (claim 4 and new claims 39-41) additives such as glidants, lubricants, silica, stearic acid etc., Blume and Dansereau teach the conventional

excipients including lubricants such as magnesium stearate, calcium stearate etc; binders such as povidone (polyvinylpyrrolidone), gelatin, starch; glidants such as talc or silicon dioxide, stabilizers and other excipients such as lactose, sorbitol etc. Accordingly, in the absence of evidence to the criticality of the specific excipients and their amounts (claims 3-4 & 33-34), it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to the choose the appropriate excipient and optimize the amounts of the same in the composition of Blume with an expectation to achieve the desired effect.

Response to Arguments

2. Applicant's arguments filed 11-17-08 have been fully considered but they are not persuasive.

3. Applicants' argument that if the resulting mixture of Blume reads on the instant agglomerated mixture, then there is no reason to combine the teachings of other references is not persuasive because it amounts to arguing the references individually. The rejection clearly explains what is lacking in Blume, for which the examiner relies on the teachings of Dansereau, Troy and Ansel. Further, examiner incorporates here response to applicants' arguments regarding the teachings of Blume and Dansereau from the last action (07-15-2008). It is also noted that instant claim 38 also recites up to 30% to be higher than 425 microns, which could possibly include 10% particles having a size greater than 2000 microns. Applicants argue that Troy is not directed to guaifenesin and instead only teaches sugar agglomerates and hence does not teach high content

guaifenesin particles of instant claims. It is argued that Ansel is even removed further because the reference fails to teach any medication. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection is made over a combination of references all of which are directed to preparing granules (in general or particularly guaifenesin) and free flowing particles in the art of pharmaceutical tablets. Thus, the cited references are analogous in art and hence the combination would flow logically. Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art. KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1395-97 (2007). Applicants argue that examiner is attempting to find isolated bits and pieces, which still does not teach the claimed invention. However, the issue to b resolved is whether the claimed invention is anticipated or obvious over the knowledge present in the relevant art. Further reliance on a number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

It is argued that the Examiner attempts to cite Troy and Ansel as showing agglomerates ranging in particle size from "about 325 to about 12 mesh" [about 1.68mm to about 44 microns-source Perry's Chemical Engineers Handbook, sixth edition, cited

in applicant's last response] and column 1, lines 59-61 of Troy. However, such teachings do not correct the deficiencies of Blume and Dansereau. Applicant's claims and particularly the particle size distribution as recited in claims 37, 38, and 42 clearly distinguish the particle size distribution as limitations of the claims. This argument is not persuasive because as explained above Troy and Ansel generally teach the preparation of tablets by compression. Troy suggests that free flowing agglomerates are prepared and segregated based on their sizes, between 12 mesh to 325 mesh (which is about 2 mm to 45 microns). In example 1, Troy suggests employing 16 mesh screen which is about 850 microns & more particularly state that agglomerates typically have a range of 20-80 mesh (850 microns-200micron) (9col. 3, L 16-20) . Troy suggests such a process for most active materials that have poor compression properties (col. 1, 20). Thus, the particle sizes of Troy inlcude the particles sizes that applicants are attempting to prepare for guaifenesin. In regards to the question if Troy teaches guaifenesin, the reference fails to exemplify but generally teaches for pharmaceutical compositions, which by necessity require an active agent. Also the example 2 is directed active agents suchas vitamin C, which reads on an active agent; and specifically mentions antitussives (includes any antitussives including guaifenesin of Blume). Thus, troy suggests not just sugar agglomerates and instead suggests active agents. Additionally, Troy also suggests that binder and other excipients for compactability (col. 3, L 50-62).

4. The argument that Ansel is removed further is not persuasive because Ansel is cited fro general teaching of preparing tablets and the types of granulations, general size ranges (smaller the tablet, smaller the granules (page211). Accordingly, even

though Ansel states "that one reason for capping of tablets is a granulation which has too great a proportion of fines or fine powder" when read in light of the above suggestion of tablet size and particle size, a skilled artisan would understand that the capping of tablets is affected by granule size. Regarding the argument that Troy teaches away from instant particle sizes, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed…." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). In this regard, Applicant's description of the prior art, page 2, lines 5-14 of the specification shows that prior art compositions had unacceptably high friability and unacceptably low hardness and tend to exhibit "capping", that is cracking and separation of part of the dosage form from the remaining body of the dosage form and it is further described at page 3 of the specification beginning at line 5 that the guaifenesin containing composition of the presently claimed invention provides improved robustness and flexibility with regard to processing conditions when the particle size distribution is such that less than about 30% by weight exhibit a particle size greater than about 425 micrometers and greater than about 80% by weight of the particles exhibit a particle size of greater than about 45 micrometers. Thus, in contrast to the argument that Ansel teaches away, the teaching of Ansel is very pertinent to the instant subject matter Ansel emphasizes the importance of particle size for free-flowing, compressing drug of good strength and the absence of capping.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611
February 2, 2009